Replaced by Article 19 13 NOV 1996

Claims

1. A chimaeric polypeptide comprising: a binding portion having specific binding affinity for a eukaryotic target cell surface component and an effector portion comprising an amino acid sequence capable of exerting a biological effect; whereby binding of the polypeptide to the cell surface component induces internalisation of at least the effector portion so as to allow the amino acid sequence to exert its biological effect.

2. A polypeptide according to claim 1, wherein the amino acid sequence is capable of exerting an immunomodulatory effect.

3. A polypeptide according to claim 1 or 2, wherein the cell surface component is an antigen or a receptor molecule.

4. A polypeptide according to any one of claims 1, 2 or 3, wherein the binding portion comprises an immunoglobulin molecule or an effective portion thereof.

5. A polypeptide according to any one of the preceding claims, wherein after internalisation the amino acid sequence is presented on the surface of the target cell in association with class I MHC antigen so as to modulate a CTL response.

6. A polypeptide according to any one of the preceding claims, wherein after internalisation the amino acid sequence is presented on the surface of the target cell in association with class II MHC antigen so as to modulate a T helper cell response.

7. A polypeptide according to any one of the preceding claims, wherein the effector portion comprises one or more immunodominant T cell peptide epitopes.

8. A polypeptide according to any one of the preceding claims, wherein the effector portion comprises a number of repeats of the same amino acid sequence capable of exerting an immunomodulatory effect.

9. A polypeptide according to any one of the preceding claims, wherein the effector portion comprises a plurality of different amino acid sequences, such that the different amino acid sequences are capable of being presented by respective MHC antigens of a different haplotype.

10. A polypeptide according to any one of the preceding claims, wherein the cell surface component is selected from the group consisting of: MHC class I antigen; MHC class II antigen; FcRI receptor; B cell surface immunoglobulin; Lewis Y antigen; TSH receptor; and the MBr1 antigen.

11. A polypeptide according to any one of the preceding claims, wherein the effector portion comprises an amino acid sequence selected from the group consisting of: MAGE 1, 2 or 3 antigens; tetanus toxin P2 peptide; the HIV-V3 loop epitope; the p53 anti-oncogene protein; influenza virus matrix protein; and influenza virus nucleoprotein.

12. A polypeptide according to any one of the preceding claims, further comprising a signal directing the amino acid sequence to a particular cellular compartment.

13. A polypeptide according to claim 12, wherein the signal is that derived from the translocation domain of a bacterial exotoxin or HIV tat protein, or the endosome-disrupting function of an adenovirus.

14. A polypeptide according to claim 13, wherein the signal is derived from the translocation domain of Pseudomonas exotoxin.

15. A polypeptide according to any one of the preceding claims, wherein the target cell is a "professional" antigen presenting cell (APC).

16. A polypeptide according to any one claims 1 to 14, wherein the target cell is an aberrant, virus-infected or otherwise diseased cell.

17. A polypeptide according to claim 16. wherein the target cell is a tumour cell.

18. A polypeptide according to claim 16 or 17, wherein the cell surface component is a tumour-associated antigen.

19. A vaccine for stimulating an immune response, comprising an effective amount of a polypeptide in accordance with any one of the preceding claims, together with a physiologically acceptable carrier substance.

20. A method of modulating the immune response of a human or animal subject, comprising administering to the subject an effective amount of a polypeptide in accordance with any one of claims 1 to 18.

21. A method according to claim 20, wherein administering the polypeptide causes the target cell to present on its surface, together with an MHC antigen, an amino acid sequence which would not normally be presented by the target cell.

22. A method according to claim 21, wherein administering the polypeptide causes the target cell to present a CTL epitope which is foreign to the subject.

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AMENDED CLAIMS

[received by the International Bureau on 26 October 1995 (26.10.95); original claims 1,2,8,9,11 and 12 amended; remaining claims unchanged (3 pages)]

1. A chimaeric polypeptide comprising: a binding portion from one source with substantial specific binding affinity for a eukaryotic target cell surface component, an optional translocation domain from another source capable of directing the chimaeric polypeptide into cytosol, and an effector portion from a further source comprising one or more peptide units of less than 30 amino acids capable of exerting a biological effect; whereby binding of the polypeptide to the cell surface component induces internalisation of the chimaeric molecule so as to allow the peptide unit(s) to be released and exert a biological effect.

2. A polypeptide according to claim 1, wherein the peptide unit(s) is capable of exerting an immunomodulatory effect.

3. A polypeptide according to claim 1 or 2, wherein the cell surface component is an antigen or a receptor molecule.

4. A polypeptide according to any one of claims 1, 2 or 3, wherein the binding portion comprises an immunoglobulin molecule or an effective portion thereof.

5. A polypeptide according to any one of the preceding claims, wherein after internalisation the amino acid sequence is presented on the surface of the target cell in association with class I MHC antigen so as to modulate a CTL response.

6. A polypeptide according to any one of the preceding claims, wherein after internalisation the amino acid sequence is presented on the surface of the target cell in association with class II MHC antigen so as to modulate a T helper cell response.

7. A polypeptide according to any one of the preceding claims, wherein the effector portion comprises one or more immunodominant T cell peptide epitopes.

8. A polypeptide according to any one of the preceding claims, wherein the effector

portion comprises a number of repeats of the same peptide unit(s) capable of exerting an immunomodulatory effect.

9. A polypeptide according to any one of the preceding claims, wherein the effector portion comprises a plurality of different peptide unit(s), such that the different peptide unit(s) are capable of being presented by respective MHC antigens of a different haplotype.

10. A polypeptide according to any one of the preceding claims, wherein the cell surface component is selected from the group consisting of: MHC class I antigen; MHC class II antigen; FcRI receptor; B cell surface immunoglobulin; Lewis Y antigen; TSH receptor; and the MBr1 antigen.

11. A polypeptide according to any one of the preceding claims, wherein the effector portion comprises a peptide unit(s) selected from the group consisting of: MAGE 1, 2 or 3 antigens; tetanus toxin P2 peptide; the HIV-V3 loop epitope; the p53 anti-oncogene protein; influenza virus matrix protein; and influenza virus nucleoprotein.

12. A polypeptide according to any one of the preceding claims, further comprising a signal directing the peptide unit(s) to a particular cellular compartment.

13. A polypeptide according to claim 12, wherein the signal is that derived from the translocation domain of a bacterial exotoxin or HIV tat protein, or the endosome-disrupting function of an adenovirus.

14. A polypeptide according to claim 13, wherein the signal is derived from the translocation domain of Pseudomonas exotoxin.

15. A polypeptide according to any one of the preceding claims, wherein the target cell is a "professional" antigen presenting cell (APC).

16. A polypeptide according to any one claims 1 to 14, wherein the target cell is an

aberrant, virus-infected or otherwise diseased cell.

17. A polypeptide according to claim 16, wherein the target cell is a tumour cell.

18. A polypeptide according to claim 16 or 17, wherein the cell surface component is a tumour-associated antigen.

19. A vaccine for stimulating an immune response, comprising an effective amount of a polypeptide in accordance with any one of the preceding claims, together with a physiologically acceptable carrier substance.

20. A method of modulating the immune response of a human or animal subject, comprising administering to the subject an effective amount of a polypeptide in accordance with any one of claims 1 to 18.

21. A method according to claim 20, wherein administering the polypeptide causes the target cell to present on its surface, together with an MHC antigen, an amino acid sequence which would not normally be presented by the target cell.

22. A method according to claim 21, wherein administering the polypeptide causes the target cell to present a CTL epitope which is foreign to the subject.

Claims

1. A chimaeric polypeptide comprising: a binding portion comprising an immunoglobulin molecule or ~~an effective~~ a portion thereof having specific binding affinity for a eukaryotic target cell surface component, and an effector portion consisting of one or more copies of an immunogenic peptide; whereby binding of the polypeptide to the cell surface component induces internalisation of at least the effector portion so as to allow the immunogenic peptide to be presented by MHC molecules on the target cell surface.

~~2. A chimaeric polypeptide comprising: a binding portion, from a first source, having specific binding affinity for a eukaryotic target cell surface component; an effector portion, from a second source, comprising a peptide capable of exerting a biological effect; and a translocation portion, from a third source, the translocation portion being adjacent to the effector portion; whereby binding of the polypeptide to the cell surface component induces internalisation of at least the effector and translocation portions so as to allow the effector portion to enter the cytosol of the target cell and thence allow the peptide to exert its biological effect.~~

3. A polypeptide according to claim ~~2~~ 1, wherein the binding portion comprises an immunoglobulin molecule or ~~an effective~~ a portion thereof.

~~4. A polypeptide according to claim 2 or 3, wherein the peptide is capable of exerting an immunomodulatory effect.~~

~~5. A polypeptide according to any one of the preceding claims, wherein the cell surface component is an antigen or a receptor molecule.~~

6. A polypeptide according to any one of the preceding claims, wherein after internalisation the peptide is presented on the surface of the target cell in association with class I MHC antigen so as to modulate a CTL response.

~~7. A polypeptide according to any one of claims 4, 5 or 6, as dependent on claim 1,~~

wherein after internalisation the peptide is presented on the surface of the target cell in association with class II MHC antigen so as to modulate a T helper cell response.

8. A polypeptide according to any one of the preceding claims, wherein the effector portion comprises one or more immunodominant T cell peptide epitopes.

9. A polypeptide according to any one of the preceding claims, wherein the effector portion comprises a number of repeats of the same peptide capable of exerting an immunomodulatory effect.

10. A polypeptide according to any one of the preceding claims, wherein the effector portion comprises a plurality of different peptides, such that the different peptides are capable of being presented by respective MHC antigens of a different haplotype.

11. A polypeptide according to any one of the preceding claims, wherein the cell surface component is selected from the group consisting of: MHC class I antigen; MHC class II antigen; FcRI receptor; B cell surface immunoglobulin; Lewis Y antigen; TSH receptor; and the MBr1 antigen.

12. A polypeptide according to any one of the preceding claims, wherein the effector portion comprises a peptide unit(s) selected from the group consisting of: MAGE 1, 2 or 3 antigens; tetanus toxin P2 peptide; the HIV-V3 loop epitope; the p53 anti-oncogene protein; influenza virus matrix protein; and influenza virus nucleoprotein.

13. A polypeptide according to any one of claims 4-12, as dependent on claim 1, further comprising a signal directing the peptide unit(s) to a particular cellular compartment.

14. A polypeptide according to any one of the preceding claims, comprising a translocation portion derived from the translocation domain of a bacterial exotoxin or HIV tat protein, or the endosome-disrupting function of an adenovirus.

15. A polypeptide according to claim 14, wherein the signal is derived from the

translocation domain of *Pseudomonas* exotoxin.

16. A polypeptide according to any one of the preceding claims, wherein the target cell is a "professional" antigen presenting cell (APC).

17. A polypeptide according to any one claims 1 to 15, wherein the target cell is an aberrant, virus-infected or otherwise diseased cell.

18. A polypeptide according to claim 17, wherein the target cell is a tumour cell.

19. A polypeptide according to claim 15 or 18, wherein the cell surface component is a tumour-associated antigen.

20. A vaccine for stimulating an immune response, comprising an effective amount of a polypeptide in accordance with any one of the preceding claims, together with a physiologically acceptable carrier substance.

21. A method of modulating the immune response of a human or animal subject, comprising administering to the subject an effective amount of a polypeptide in accordance with any one of claims 1 to 19.

22. A method according to claim 21, wherein administering the polypeptide causes the target cell to present on its surface, together with an MHC antigen, an amino acid sequence which would not normally be presented by the target cell.

23. A method according to claim 22, wherein administering the polypeptide causes the target cell to present a CTL epitope which is foreign to the subject.